

## We Claim:

1. A method of identifying a compound that is capable of modulating feeding behavior, fat deposition, metabolic rate, or the ratio of lean muscle mass to body fat in a subject, said method comprising performing an assay to measure a metabolism-associated phenotype that has been determined for a genetically modified non-human animal that comprises a genetic modification within an allele of its Cbl locus wherein said genetic modification reduces or prevents expression of a functional endogenous Cbl in said animal, and wherein said assay is conducted in the presence and absence of a compound to be tested; and determining the effect of the compound on the phenotype wherein a modified phenotype indicates that the compound is capable of modulating feeding behavior, fat deposition, metabolic rate, or the ratio of lean muscle mass to body fat in a subject.
2. The method according to claim 1 wherein the assay to determine a metabolism-associated phenotype measures Cbl-mediated ubiquitination of the insulin receptor in the presence and absence of the compound.
3. The method according to claim 2 wherein the assay comprises:
  - (a) providing a cell that is capable of effecting the c-Cbl-mediated ubiquitination of the insulin receptor;
  - (b) incubating the cell in the presence and absence of a compound to be tested; and
  - (c) determining c-Cbl-mediated ubiquitination of the insulin receptor in the presence and absence of the compound wherein a modified level of c-Cbl-mediated ubiquitination of the insulin receptor indicates that the compound is capable of modulating feeding behavior, fat deposition, metabolic rate, or the ratio of lean muscle mass to body fat in a subject.
4. The method according to claim 3 wherein the compound reduces or inhibits Cbl-mediated ubiquitination of the insulin receptor thereby indicating that said compound is capable of enhancing feeding behavior in a subject.

5. The method according to claim 3 wherein the compound reduces or inhibits Cbl-mediated ubiquitination of the insulin receptor thereby indicating that said compound is capable of reducing fat deposition in a subject.
- 5 6. The method according to claim 3 wherein the compound reduces or inhibits Cbl-mediated ubiquitination of the insulin receptor thereby indicating that said compound is capable of enhancing metabolic rate in a subject.
- 10 7. The method according to claim 3 wherein the compound reduces or inhibits Cbl-mediated ubiquitination of the insulin receptor thereby indicating that said compound is capable of enhancing the ratio of lean muscle mass to body fat in a subject.
- 15 8. The method according to claim 3 wherein the compound enhances or agonizes Cbl-mediated ubiquitination of the insulin receptor thereby indicating that said compound is capable of reducing feeding behavior and/or enhancing fat deposition in a subject and/or reducing metabolic rate in a subject and/or reducing the ratio of lean muscle mass to body fat in a subject.
- 20 9. The method according to claim 3 comprising performing an immunoassay wherein the level of c-Cbl-mediated ubiquitination of the insulin receptor is determined by contacting the insulin receptor with an antibody that binds to ubiquitin under conditions sufficient for an antigen-antibody complex to form and detecting the antibody bound to the receptor.
- 25 10. The method according to claim 9 further comprising contacting the insulin receptor with an antibody that binds to the insulin receptor under conditions sufficient for an antigen-antibody complex to form.
- 30 11. The method according to claim 3 comprising performing an immunoassay by a process comprising:
  - (a) providing a cell that is capable of effecting the c-Cbl-mediated ubiquitination of the insulin receptor;
  - (b) incubating the cell in the presence and absence of a compound to be tested;

- (c) contacting an extract of the cell comprising the insulin receptor with an antibody that binds to the insulin receptor under conditions sufficient for an antigen-antibody complex to form thereby capturing the insulin receptor;
- (d) contacting the captured insulin receptor with an antibody that binds to ubiquitin under conditions sufficient for an antigen-antibody complex to form; and
- (e) detecting the antibody bound at (d).

12. The method according to claim 11 wherein the antibody bound at (d) is detected by contacting the antibody with a tertiary antibody that is capable of producing a detectable signal.

13. The method according to claim 1 wherein the assay to determine a metabolism-associated phenotype measures phosphorylation of a tyrosine residue on Cbl protein in the presence and absence of the compound.

14. The method according to claim 1 wherein the assay to determine a metabolism-associated phenotype measures the amount of Cbl protein in the cell in the presence and absence of the compound.

15. The method according to claim 14 wherein the assay comprises:

- (a) providing a cell that is capable of expressing c-Cbl protein;
- (b) incubating the cell in the presence and absence of a compound to be tested; and
- (c) determining amount of c-Cbl protein in the cell in the presence and absence of the compound wherein a modified level of c-Cbl protein indicates that the compound is capable of modulating feeding behavior, fat deposition, metabolic rate, or the ratio of lean muscle mass to body fat in a subject.

16. The method according to claim 15 wherein the compound reduces or inhibits Cbl expression as determined by a reduced amount of Cbl protein in the cell thereby indicating that said compound is capable of enhancing feeding behavior in a subject.

17. The method according to claim 15 wherein the compound reduces or inhibits Cbl expression as determined by a reduced amount of Cbl protein in the cell thereby indicating that said compound is capable of reducing fat deposition in a subject.
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18. The method according to claim 15 wherein the compound reduces or inhibits Cbl expression as determined by a reduced amount of Cbl protein in the cell thereby indicating that said compound is capable of enhancing metabolic rate in a subject.
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19. The method according to claim 15 wherein the compound reduces or inhibits Cbl expression as determined by a reduced amount of Cbl protein in the cell thereby indicating that said compound is capable of enhancing the ratio of lean muscle mass to body fat in a subject.
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20. The method according to claim 15 wherein the compound enhances or agonizes Cbl expression as determined by an increased amount of Cbl protein in the cell thereby indicating that said compound is capable of reducing feeding behavior and/or enhancing fat deposition in a subject and/or reducing metabolic rate in a subject and/or reducing the ratio of lean muscle mass to body fat in a subject.
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21. The method according to claim 15 comprising performing an immunoassay wherein the amount of c-Cbl is determined by contacting the Cbl protein with an antibody that binds to Cbl under conditions sufficient for an antigen-antibody complex to form and detecting the antibody bound to the Cbl protein.
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22. The method according to claim 21 wherein the antibody bound to the Cbl protein is detected by contacting the antibody with a secondary antibody that is capable of producing a detectable signal.
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23. The method according to claim 15 comprising performing an immunoassay wherein the amount of c-Cbl is determined by contacting the Cbl protein with a primary and secondary antibody that each bind to Cbl under conditions

sufficient for antigen-antibody complexes to form and detecting an antibody bound to the Cbl protein.

24. The method according to claim 23 wherein the antibody bound to the Cbl protein is detected by contacting the antibody with a secondary antibody that is capable of producing a detectable signal.
25. The method according to claim 23 wherein the primary and secondary antibody bind to different epitopes on the Cbl protein.
26. The method according to claim 15 comprising performing an immunoassay by a process comprising:
- (a) providing a cell that is capable of expressing c-Cbl protein;
  - (b) incubating the cell in the presence and absence of a compound to be tested;
  - (c) contacting an extract of the cell comprising the Cbl protein with an antibody that binds to Cbl protein under conditions sufficient for an antigen-antibody complex to form thereby capturing the Cbl protein; and
  - (d) detecting the antibody bound at (e).
27. The method according to claim 15 comprising performing an immunoassay by a process comprising:
- (a) providing a cell that is capable of expressing c-Cbl protein;
  - (b) incubating the cell in the presence and absence of a compound to be tested;
  - (c) contacting an extract of the cell comprising the Cbl protein with an antibody that binds to Cbl protein under conditions sufficient for an antigen-antibody complex to form thereby capturing the Cbl protein;
  - (d) contacting the captured Cbl protein with an antibody that binds to Cbl protein under conditions sufficient for an antigen-antibody complex to form, wherein said antibody binds to a different epitope on Cbl to the antibody at (c); and
  - (e) detecting the antibody bound at (d).
28. The method according to claim 26 or 27 wherein the antibody is detected by contacting the antibody with an antibody that is capable of producing a detectable signal.

29. The method according to claim 1 wherein the assay to determine a metabolism-associated phenotype measures Cbl-mediated fat and/or glucose metabolism in the cell in the presence and absence of the compound.
- 5 30. The method according to claim 29 wherein the assay to determine a metabolism-associated phenotype measures a phenotype in the presence and absence of the compound selected from the group consisting of fat mass, glucose transport, muscle thermogenesis, mitochondrial structure, mitochondrial function, and mitochondrial respiration rate.
- 10 31. The method according to claim 29 or 30 wherein the assay measures muscle thermogenesis in the cell in the presence and absence of the compound.
- 15 32. The method according to claim 31 wherein muscle thermogenesis in the presence and absence of the compound is determined by a process comprising determining the proton leak kinetics of a cell in the presence and absence of the compound.
- 20 33. The method according to claim 32 comprising:
- (a) providing a cell of myoblast lineage capable of expressing c-Cbl protein;
  - (b) incubating the cell in the presence and absence of a compound to be tested; and
  - (c) determining the respiration rate and/or membrane potential of the cell in the presence and absence of the compound wherein a modified respiration rate and/or membrane potential indicates that the compound is capable of modulating feeding behavior, fat deposition, metabolic rate, or the ratio of lean muscle mass to body fat in a subject.
- 25 34. The method according to claim 33 wherein the compound enhances respiration rate and/or membrane potential of the cell thereby indicating that said compound is capable of enhancing feeding behavior in a subject.
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35. The method according to claim 33 wherein the compound enhances respiration rate and/or membrane potential of the cell thereby indicating that said compound is capable of reducing fat deposition in a subject.
- 5 36. The method according to claim 33 wherein the compound enhances respiration rate and/or membrane potential of the cell thereby indicating that said compound is capable of enhancing metabolic rate in a subject.
- 10 37. The method according to claim 33 wherein the compound enhances respiration rate and/or membrane potential of the cell thereby indicating that said compound is capable of enhancing the ratio of lean muscle mass to body fat in a subject.
- 15 38. The method according to claim 33 wherein the compound reduces or inhibits respiration rate and/or membrane potential of the cell thereby indicating that said compound is capable of reducing feeding behavior and/or enhancing fat deposition in a subject and/or reducing metabolic rate in a subject and/or reducing the ratio of lean muscle mass to body fat in a subject.
- 20 39. The method according to claim 29 or 30 wherein the assay comprises:
- (a) providing a compound to be tested to an animal subject that expresses a functional Cbl protein; and
  - (b) determining a metabolism-associated phenotype in a cell or tissue of the animal wherein a modified phenotype in the presence of the compound
- 25 indicates that the compound is capable of modulating feeding behavior, fat deposition, metabolic rate, or the ratio of lean muscle mass to body fat in a subject.
- 30 40. The method according to claim 39 wherein the metabolism-associated phenotype is selected from the group consisting of fat mass, glucose transport, muscle thermogenesis, mitochondrial structure, mitochondrial function, and mitochondrial respiration rate.

41. The method according to claim 40 wherein the metabolism-associated phenotype is muscle thermogenesis.

5 42. The method according to claim 41 wherein muscle thermogenesis in the presence of the compound is determined by a process comprising determining the proton leak kinetics of a cell or tissue of the animal.

10 43. The method according to claim 41 or 42 wherein muscle thermogenesis is determined by measuring the respiration rate and/or membrane potential of a cell from the animal wherein a modified respiration rate and/or membrane potential indicates that the compound is capable of modulating feeding behavior, fat deposition, metabolic rate, or the ratio of lean muscle mass to body fat in a subject.

15 44. The method according to claim 43 wherein the compound enhances respiration rate and/or membrane potential of the cell thereby indicating that said compound is capable of enhancing feeding behavior in a subject.

20 45. The method according to claim 43 wherein the compound enhances respiration rate and/or membrane potential of the cell thereby indicating that said compound is capable of reducing fat deposition in a subject.

25 46. The method according to claim 43 wherein the compound enhances respiration rate and/or membrane potential of the cell thereby indicating that said compound is capable of enhancing metabolic rate in a subject.

30 47. The method according to claim 43 wherein the compound enhances respiration rate and/or membrane potential of the cell thereby indicating that said compound is capable of enhancing the ratio of lean muscle mass to body fat in a subject.

48. The method according to claim 43 wherein the compound reduces or inhibits respiration rate and/or membrane potential of the cell thereby indicating that said compound is capable of reducing feeding behavior and/or enhancing fat



deposition in a subject and/or reducing metabolic rate in a subject and/or reducing the ratio of lean muscle mass to body fat in a subject.

49. The method according to claim 39 wherein the animal subject is a non-human animal subject.

50. The method according to claim 49 wherein the non-human animal subject expresses an endogenous native Cbl protein.

51. The method according to claim 49 wherein the non-human animal subject expresses an introduced human Cbl protein.

52. The method according to claim 49 wherein the non-human animal is a mammal.

53. The method according to claim 52 wherein the mammal is selected from the group consisting of rodent, dog, pig, bovine, sheep, horse and goat.

54. The method according to claim 53 wherein the rodent is selected from the group consisting of rabbit, rat, guinea pig and mouse.

55. The method according to claim 54 wherein the rodent is a mouse.

56. The method according to claim 39 wherein the compound is administered to muscle tissue of the animal subject.

57. The method according to claim 56 wherein the metabolism-associated phenotype is determined in muscle tissue of the animal subject.

58. The method according to claim 1 comprising comparing the effect of the compound on the metabolism-associated phenotype to a metabolism-associated phenotype for a genetically modified non-human animal that comprises a genetic modification within an allele of its Cbl locus wherein said genetic modification reduces or prevents expression of a functional

endogenous Cbl in said animal, and wherein the ability of the compound to mimic or reproduce the phenotype of the genetically modified non-human animal indicates that the compound is capable of enhancing feeding behavior and/or reducing fat deposition and/or enhancing metabolic rate and/or enhancing the ratio of lean muscle mass to body fat in a subject.

59. The method according to claim 1 comprising comparing the effect of the compound on the metabolism-associated phenotype to a metabolism-associated phenotype for a non-human animal that expresses a functional Cbl protein, and wherein the ability of the compound to mimic or reproduce the phenotype of the non-human animal indicates that the compound is capable of reducing feeding behavior and/or enhancing fat deposition and/or reducing metabolic rate and/or reducing the ratio of lean muscle mass to body fat in a subject.

60. A method of identifying a compound that suppresses or reduces feeding behavior, said method comprising:

- (a) administering a compound to a genetically modified non-human animal comprising a genetic modification within an allele of its Cbl locus wherein said genetic modification reduces or prevents expression of a functional endogenous Cbl in said animal; and
- (b) determining the feeding behavior of the animal, wherein reduced appetite or dietary intake of the animal compared to the appetite or dietary intake of a Cbl-deficient animal to which the compound has not been administered indicates that the compound suppresses or reduces feeding behavior.

61. A method for identifying a compound that suppresses or reduces feeding behavior, said method comprising determining the ubiquitin ligase activity of a Cbl protein in the presence and absence of the compound wherein enhanced ubiquitin ligase activity of the Cbl protein in the presence of the compound indicates that the compound suppresses or reduces feeding behavior.

62. A method for identifying a compound that suppresses or reduces feeding behavior comprising determining the level of tyrosine phosphorylation of a Cbl

protein in the presence and absence of the compound wherein enhanced phosphorylation of tyrosine residues in the Cbl protein in the presence of the compound indicates that the compound suppresses or reduces feeding behavior.

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63. A method of identifying a compound that enhances feeding behavior said method comprising:

(a) administering a compound that suppresses appetite or dietary intake to a genetically modified non-human animal comprising a genetic modification within an allele of its Cbl locus wherein said genetic modification reduces or prevents expression of a functional endogenous Cbl in said animal and determining the feeding behavior of the animal;

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(b) administering a compound to the animal and determining the feeding behavior of the animal, wherein enhanced appetite or dietary intake at (b) compared to (a) indicates that the compound enhances feeding behavior.

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64. A method of identifying a compound that enhances feeding behavior comprising determining the ubiquitin ligase activity of a Cbl protein in the presence and absence of the compound wherein reduced ubiquitin ligase activity of the Cbl protein in the presence of the compound indicates that the compound enhances feeding behavior.

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65. A method for identifying a compound that enhances feeding behavior comprising determining the level of tyrosine phosphorylation of a Cbl protein in the presence and absence of the compound wherein reduced phosphorylation of tyrosine residues in the Cbl protein in the presence of the compound indicates that the compound enhances feeding behavior.

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66. A method of identifying a compound that modulates feeding behavior, said method comprising:

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(a) administering a compound to a non-human animal expressing a functional Cbl protein and determining the feeding behavior of the animal;

(b) determining the feeding behavior of a genetically modified non-human animal comprising a genetic modification within an allele of its Cbl locus wherein said

genetic modification reduces or prevents expression of a functional endogenous Cbl in said animal; and

- (c) comparing the feeding behavior of the animals at (a) and (b) wherein a comparable feeding behavior between (a) and (b) indicates that the compound modulates feeding behavior.

67. A method of identifying a compound that modulates feeding behavior comprising determining the ubiquitin ligase activity of a Cbl protein in the presence and absence of the compound wherein modified ubiquitin ligase activity of the Cbl protein in the presence of the compound indicates that the compound enhances feeding behavior.

68. A method for identifying a compound that modulates feeding behavior comprising determining the level of tyrosine phosphorylation of a Cbl protein in the presence and absence of the compound wherein modified phosphorylation of tyrosine residues in the Cbl protein in the presence of the compound indicates that the compound modulates feeding behavior.

69. A method of identifying a compound that enhances fat deposition or reduces lean muscle mass or enhances the ratio of body fat to muscle or reduces metabolic rate, said method comprising:

- (a) administering a compound to a genetically modified non-human animal comprising a genetic modification within an allele of its Cbl locus wherein said genetic modification reduces or prevents expression of a functional endogenous Cbl in said animal; and
- (b) determining the fat content of the animal, wherein enhanced fat content of the animal compared to the fat content of a Cbl-deficient animal to which the compound has not been administered indicates that the compound enhances fat deposition or reduces lean muscle mass or enhances the ratio of body fat to muscle or reduces metabolic rate.

70. A method of identifying a compound that enhances fat deposition or reduces lean muscle mass or enhances the ratio of body fat to muscle or reduces metabolic rate comprising determining the ubiquitin ligase activity of a Cbl

protein in the presence and absence of the compound wherein enhanced ubiquitin ligase activity of the Cbl protein in the presence of the compound indicates that the compound enhances fat deposition or reduces lean muscle mass or enhances the ratio of body fat to muscle or reduces metabolic rate.

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71. A method for identifying a compound that enhances fat deposition or reduces lean muscle mass or enhances the ratio of body fat to muscle or reduces metabolic rate comprising determining the level of tyrosine phosphorylation of a Cbl protein in the presence and absence of the compound wherein enhanced phosphorylation of tyrosine residues in the Cbl protein in the presence of the compound indicates that the compound enhances fat deposition or reduces lean muscle mass or enhances the ratio of body fat to muscle or reduces metabolic rate.

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72. A method of identifying a compound that reduces fat deposition or enhances lean muscle mass or reduces the ratio of body fat to muscle or enhances metabolic rate, said method comprising:
- (a) administering a compound that enhances fat deposition or glucose uptake to a genetically modified non-human animal comprising a genetic modification within an allele of its Cbl locus wherein said genetic modification reduces or prevents expression of a functional endogenous Cbl in said animal and determining the fat content of the animal; and
  - (b) administering a compound to the animal and determining the fat content of the animal, wherein a similar or reduced fat content at (b) compared to (a) indicates that the compound reduces fat deposition or enhances lean muscle mass or reduces the ratio of body fat to muscle or enhances metabolic rate.

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73. A method of identifying a compound that reduces fat deposition or enhances lean muscle mass or reduces the ratio of body fat to muscle or enhances metabolic rate comprising:
- (a) administering a compound to a non-human animal expressing a functional Cbl protein and determining the fat content of the animal;
  - (b) determining the fat content of a genetically modified non-human animal comprising a genetic modification within an allele of its Cbl locus wherein said

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genetic modification reduces or prevents expression of a functional endogenous Cbl in said animal; and

- (c) comparing the fat contents of the animals at (a) and (b) wherein a comparable fat content between (a) and (b) indicates that the compound reduces fat deposition or enhances lean muscle mass or reduces the ratio of body fat to muscle or enhances metabolic rate.

74. A method of identifying a compound that reduces fat deposition or enhances lean muscle mass or reduces the ratio of body fat to muscle or enhances metabolic rate comprising determining the ubiquitin ligase activity of a Cbl protein in the presence and absence of the compound wherein reduced ubiquitin ligase activity of the Cbl protein in the presence of the compound indicates that the compound reduces fat deposition or enhances lean muscle mass or reduces the ratio of body fat to muscle or enhances metabolic rate.

75. A method for identifying a compound that reduces fat deposition or enhances lean muscle mass or reduces the ratio of body fat to muscle or enhances metabolic rate comprising determining the level of tyrosine phosphorylation of a Cbl protein in the presence and absence of the compound wherein reduced phosphorylation of tyrosine residues in the Cbl protein in the presence of the compound indicates that the compound reduces fat deposition or enhances lean muscle mass or reduces the ratio of body fat to muscle or enhances metabolic rate.

76. A method of identifying a compound that enhances glucose uptake, said method comprising:

- (a) administering a compound to a genetically modified non-human animal comprising a genetic modification within an allele of its Cbl locus wherein said genetic modification reduces or prevents expression of a functional endogenous Cbl in said animal; and
- (b) determining the glucose uptake into liver, fat or muscle cells of the animal, wherein enhanced uptake compared to the glucose uptake into liver, fat or muscle cells of a Cbl-deficient animal to which the compound has not been administered indicates that the compound enhances glucose uptake.

77. A method of identifying a compound that enhances glucose uptake comprising determining the ubiquitin ligase activity of a Cbl protein in the presence and absence of the compound wherein reduced ubiquitin ligase activity of the Cbl protein in the presence of the compound indicates that the compound reduces fat deposition or enhances glucose uptake.

78. A method for identifying a compound that enhances glucose uptake comprising determining the level of tyrosine phosphorylation of a Cbl protein in the presence and absence of the compound wherein reduced phosphorylation of tyrosine residues in the Cbl protein in the presence of the compound indicates that the compound enhances glucose uptake.

79. A method of identifying a compound that reduces glucose uptake into liver, fat or muscle cells, said method comprising:

- (a) administering a compound that enhances glucose uptake to a genetically modified non-human animal comprising a genetic modification within an allele of its Cbl locus wherein said genetic modification reduces or prevents expression of a functional endogenous Cbl in said animal and determining the glucose uptake into liver, fat or muscle cells;
- (b) administering a compound to the animal and determining the glucose uptake into liver, fat or muscle cells of the animal, wherein a similar or reduced uptake at (b) compared to (a) indicates that the compound reduces glucose uptake into liver, fat or muscle cells.

80. A method of identifying a compound that reduces glucose uptake into liver, fat or muscle cells comprising:

- (a) administering a compound to a non-human animal expressing a functional Cbl protein and determining the glucose uptake into liver, fat or muscle cells of the animal;
- (b) determining the glucose uptake into liver, fat or muscle cells of a genetically modified non-human animal comprising a genetic modification within an allele of its Cbl locus wherein said genetic modification reduces or prevents expression of a functional endogenous Cbl in said animal; and

- (c) comparing the glucose uptake into liver, fat or muscle cells of the animals at (a) and (b) wherein a comparable uptake between (a) and (b) indicates that the compound reduces glucose uptake into liver, fat or muscle cells.

5 81. A method of identifying a compound that reduces glucose uptake comprising determining the ubiquitin ligase activity of a Cbl protein in the presence and absence of the compound wherein enhanced ubiquitin ligase activity of the Cbl protein in the presence of the compound indicates that the compound reduces glucose uptake.

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82. A method for identifying a compound that reduces glucose uptake comprising determining the level of tyrosine phosphorylation of a Cbl protein in the presence and absence of the compound wherein enhanced phosphorylation of tyrosine residues in the Cbl protein in the presence of the compound indicates that the compound reduces glucose uptake.

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83. The method according to any one of claims 1 to 82 wherein the compound being tested is a protein.

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84. The method according to claim 83 wherein the protein is a dominant negative mutant of Cbl.

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85. The method according to claim 84 wherein the dominant negative mutant of Cbl comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 248, SEQ ID NO: 250, SEQ ID NO: 252, SEQ ID NO: 254, SEQ ID NO: 256, SEQ ID NO: 258 and SEQ ID NO: 260.

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84. The method according to any one of claims 1 to 83 wherein the compound being tested is nucleic acid.

85. The method according to claim 84 wherein the nucleic acid comprises an antisense molecule, ribozyme, siRNA, or shRNA.



86. The method according to claim 85 wherein the nucleic acid comprises siRNA, or shRNA that comprises a nucleotide sequence set forth in any one of SEQ ID NOS: 4-239.
- 5 87. The method according to any one of claims 1 to 83 wherein the compound tested is a small organic molecule.
88. The method according to any one of claims 1 to 83 wherein the compound is an antibody that binds to a Cbl protein.
- 10 89. The method according to any one of claims 1 to 88 further comprising formulating the identified compound for administration to a non-human animal or a human.
- 15 90. The method according to any one of claims 1 to 89 further comprising producing or synthesizing the compound.
91. A process for identifying or determining a compound that modulates feeding behavior, fat deposition, metabolic rate, or the ratio of lean muscle mass to body fat in a subject, said process comprising:
- 20 (a) performing the method according to any one of claims 1 to 90;
- (b) optionally, determining the structure of the compound; and
- (c) providing the compound or the name or structure of the compound.
- 25 92. The process according to claim 91 wherein the compound name or structure is provided in a paper form, machine-readable form, or computer-readable form.
93. The process according to claim 90 or 91 wherein the compound structure is known.
- 30 94. The process according to any one of claims 90 to 92 wherein the compound or the name or structure of the compound is provided with an indication as to its use.

95. A process for producing a compound that modulates feeding behavior, fat deposition, metabolic rate, or the ratio of lean muscle mass to body fat in a subject, said process comprising:

- (a) performing the method according to any one of claims 1 to 90 to thereby identify or determine a compound;
- (b) optionally, determining the structure of the compound or modulator;
- (c) optionally, providing the name or structure of the compound or modulator; and
- (d) producing the compound or modulator.

96. The process according to claim 95 wherein the compound name or structure is provided in a paper form, machine-readable form, or computer-readable form.

97. The process according to claim 95 or 96 wherein the compound or the name or structure of the compound is provided with an indication as to its use.

98. The process according to claim 97 further comprising formulating the compound in a suitable diluent or excipient.

99. Use of an isolated siRNA or shRNA comprising a nucleotide sequence set forth in any one of SEQ ID Nos: 4-239 to modulate a metabolism-associated phenotype in a cell, tissue or animal subject.

100. Use of a isolated nucleic acid molecule comprising a nucleotide sequence set forth in any one of SEQ ID Nos: 247, 249, 252, 253, 255, 257, or 259 to produce a dominant negative inhibitor molecule capable of modulating a metabolism-associated phenotype in a cell, tissue or animal subject.

101. Use according to claim 99 or 100 wherein the modulation to a metabolism-associated phenotype is selected from the group consisting of:

- (a) inhibition or decrease of Cbl-mediated ubiquitination of an insulin receptor;
- (b) inhibition or decrease in Cbl protein level; and
- (c) enhanced muscle thermogenesis.